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Informatics in Neuro-critical Care: New Ideas for Big Data

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Informatics in Neuro-critical Care: New Ideas for Big Data

ABSTRACT

Purpose of review

Big data is the new hype in business and healthcare. Data storage and processing has become cheap, fast, and easy. Business analysts and scientists are trying to design methods to mine these data for hidden knowledge. Neuro-critical care is a field that typically produces large amounts of patient-related data, and these data are increasingly being digitized and stored. This review will try to look beyond the hype, and focus on possible applications in neuro-intensive care amenable to Big Data research that can potentially improve patient care.

Recent findings

The first challenge in Big Data research will be the development of large, multicenter and high quality databases. These databases could be used to further investigate recent findings from mathematical models, developed in smaller datasets. Randomized clinical trials (RCTs) and Big Data research are complementary. Big Data research might be used to identify subgroups of patients that could benefit most from a certain intervention, or can be an alternative in areas where RCTs are not possible.

Summary

The processing and the analysis of the large amount of patient-related information stored in clinical databases is beyond normal human cognitive ability. Big Data research applications have the potential to discover new medical knowledge, and improve care in the neuro-intensive care unit.

Keywords

Big data; neuro-critical care; neuro-informatics; data mining; predictive modelling

INTRODUCTION

'Big data' refers to the current speed and volume at which computerized data are generated by web applications and by the digitization of information that was previously available on paper only. Additionally, it refers to the improvements in technology that enable to store, process, and analyze these data [1]. Informally, these characteristics are referred to as the 'the three V's of big data: Volume, Velocity, and Variety [2]. Surprisingly, nowadays it is more cost-effective to invest in data storage than in cleaning old databases [3]. However, the lack of standardization and the uncertain data quality has added a fourth V for 'Veracity' to the definition. Finally, Big Data is useless without a clear vision and knowledge of the 'Value' it will bring to business or healthcare [1]. Together, Volume, Velocity, Variety, Veracity and Value are the five V's of Big Data (table 1).

The intensive care unit (ICU) is a very data rich environment, where patients are monitored continuously and receive vital support [4]. This is especially true for the neuro-critical care unit, where radiological imaging and specific invasive and non-invasive bedside monitors, further contribute to the huge amounts of data collected [5–7]. Digitized medical and pharmaceutical data, when integrated, are an enormous and continuous data source, which is dwarfed by the further inclusion of data from genomics [8] or microbiomics [9]. In a structured healthcare database, the relationship between specific clinical characteristics of patients, interventions, and outcomes can be investigated at a scale that was not possible

before. Data from non-medical sources such as social networks, wearables that track daily activity and fitness, and social security or government databases could be integrated and used to assess pre-morbid status or post-hospitalization functional outcomes. Theoretically, a continuously adapting healthcare system could be designed [10] that uses these huge amounts of data to forecast the best treatment action or prognosis for each patient. Furthermore, such a system could contribute to medical knowledge and generate new research hypotheses. The technological feat of setting up such an advanced healthcare system is further challenged by proprietary, legal and privacy issues. Most importantly, the true challenge of big data research will begin after these practical obstacles have been overcome: how will these data be turned into information, knowledge and wisdom? [11] The naïve approach of over-confidence in the quality of data, and blindly applying black box techniques to address research questions, is an oversimplification that can possibly lead to dubious results and spurious interpretations. A famous quote by Dr. Isaac Kohane, Big Data pioneer and co-director of the Center for Biomedical Informatics at Harvard Medical School, is a good summary of this challenge: "You really need to know something about medicine. If statistics lie, then Big Data can lie in a very, very big way". [12]

Big Data research is still in its infancy, and clinical applications specifically for the neuro-ICU are currently lacking. Therefore, this review focuses on possible applications in the neuro-ICU amenable to Big Data research, and will discuss perspectives, opportunities and pitfalls.

CLINICAL DATA SYSTEMS AND DATABASES IN NEURO-CRITICAL CARE: STATUS AND CHALLENGES

Big Data research in the neuro-ICU will require the creation of multicenter, multi-patient and multidimensional databases. ICU's and neuro-ICU's are increasingly implementing electronic healthcare records [13]. However, standardization is lacking at many levels. First, specific to the neuro-ICU is the use of brain multimodality monitoring (MMM) [6], the simultaneous collection of data from diverse monitors in a single patient [14], such as intracranial pressure (ICP), cerebral perfusion pressure (CPP), cerebrovascular autoregulation, brain tissue oxygenation, cerebral blood flow (CBF), microdialysis, or electro-encephalography (EEG). Different centers have different preferences in the use of medical devices and/or software systems, and there is no universal standard for device communication [15], nor for synchronization between these devices [16]. There are no guidelines on the optimal resolution in which to store time series data. Inherent to the use of continuous non-validated monitoring data are artifacts and missing data, for which several automated methods for de-noising and imputation have been proposed [15] including the use of advanced data mining techniques [17]. Second, the diagnosis and management of acute brain injury relies heavily on repeated neuro-imaging, such as CT, MRI, or more advanced methods. Apart from a lack of standardization on timing, frequency, and indications, summarizing this high resolution visual information is challenging. Third, genomics data are likely to enter the neuro-ICU in the upcoming years [18,19]. Fourth, the modalities, frequency, and timing of outcome assessment are not standardized and might vary between centers, with the further limitation of a proportion patients who are inevitably lost to follow-up. For traumatic brain injury (TBI), Maas et al. have introduced recommendations to standardize the process of data collection [20]. Figure 1 is a schematic representation of the relevant healthcare information that could be collected during and after the admission of a patient to the neuro-ICU.

Existing clinical databases suffer from multiple problems. The International Mission for Prognosis And Clinical Trial (IMPACT) database, contains records of 9205 ICU patients collected between 1984-1997, but includes only few imaging data and no monitoring data [21]. The BrainIT database includes demographic,

clinical data, and minute-by-minute monitoring data as well as outcome data, but only from a very small sample of 202 patients with TBI, collected in 18 European centers between July 2003 and June 2005 [22]. Some centers are storing the data of their own patients, but do not provide access. The MIMIC II database is likely the most amenable for Big Data: it is a large open-access clinical database, however from a single not specifically neuro-ICU center. The MIMIC II database contains demographics, physiological data, medications and outcome recorded from more than 30,000 ICU patients admitted to Beth Israel Deaconess Medical Center (Boston, MA) from 2001 to 2008 [23]. The International Initiative for Traumatic Brain Injury Research (InTBIR) has developed the Federal Interagency TBI Research (FITBIR) Informatics System platform, allowing data sharing across the entire TBI community [24]. FITBIR aims to collect patient-level phenotypic, genomic, and imaging information. Additionally, embedded in the network of InTBIR, Center-TBI is currently collecting highly detailed information from 1800 ICU patients, including imaging and long-term outcomes [25].

BIG DATA RESEARCH AND THE MULTIMODALITY MONITORING PLATFORM: PERSPECTIVES AND POSSIBLE APPLICATIONS

Accumulating evidence suggests that the information obtained from MMM could be used for patient-specific therapy [7]. However, there is little guidance on what and when to monitor. Furthermore, the interpretation of the amount of sophisticated data produced by MMM is beyond normal human cognitive ability. There is a crucial need for a better understanding of the complex variability and interactions between physiological variables to transform them into usable information that can be integrated into patient care. [26] In relatively small mainly retrospective clinical studies, advanced mathematical techniques, and machine learning models, have been applied to investigate the treatment thresholds, the underlying pathophysiology, or the interactions between monitored parameter. Although they have resulted in physiologically plausible hypotheses, it would be very difficult or even impossible to study these novel insights in randomized controlled trials (RCTs). Big Data offers new insights and the possibility to extract knowledge from raw data, a process called knowledge discovery [27,28]. In what follows, work in relatively small datasets that could benefit from Big Data is discussed.

Intracranial pressure: towards individualized thresholds?

ICP monitoring is probably the most commonly applied invasive brain-specific monitor in the neuro-ICU, especially in TBI. The recommendations of the Brain Trauma Foundation guidelines to monitor ICP in every salvageable patient with severe TBI with intracranial abnormalities, and to treat ICP at a threshold of 20 mmHg [29] have been challenged by RCTs that failed to demonstrate the benefit of such a strategy [30,31]. Instead, patient-specific thresholds may be preferable. In a retrospective single center cohort study, Vik et al. have demonstrated that the area under the ICP curve above 20 mmHg, or the “dose” of intracranial hypertension, was associated with poor outcome [32]. Lazaridis et al. could demonstrate that individualized doses of intracranial hypertension, based on the cerebrovascular autoregulatory status, were stronger predictors of death than doses derived from fixed thresholds of 20 and 25 mm Hg [33]. By examining the univariate association between episodes of elevated ICP of increasing intensity and duration with outcome, Güiza et al. were able to visualize the pressure and time burden of ICP [34]. In addition, they were able to demonstrate that the ability to tolerate episodes of increased ICP depends on the age, the CPP and the cerebrovascular autoregulatory status of the patients.

Cerebrovascular autoregulation.

Cerebrovascular autoregulation is the mechanism that maintains a stable cerebral blood flow despite fluctuations in CPP. Failure of cerebrovascular autoregulation is observed in acute brain injury due to a variety of causes, such as TBI [35], subarachnoid hemorrhage (SAH) [36], stroke [37], cardiac arrest [38], and sepsis [39]. Such failure is associated with worse outcomes, and represents a challenge for hemodynamic optimization. Several methods have been proposed to assess autoregulation in a non-continuous way [36,40]. Marek Czosnyka and colleagues have pioneered the design of computational methods to assess cerebrovascular motor activity [41]. Their pressure reactivity index (PrX) calculates a moving correlation coefficient between arterial blood pressure (ABP) and ICP, using a moving window of continuous waveform data [42]. Using the PrX, the optimal CPP when autoregulation is most active can be calculated [43]. In a retrospective study, an actual CPP close to this optimal CPP, was associated with better outcomes in TBI patients [44]. The low-frequency autoregulation index (LAx) [45] was instead designed based on minute-by-minute data and was able to confirm in a retrospective study, that actual CPP close to optimal CPP was associated with better outcomes in TBI. Unfortunately, optimal CPP cannot be calculated continuously for all patients [46]. A single-center pilot study has shown the feasibility of targeted CPP management at bedside in a small adult population [47].

Early warning models for secondary injury.

Prevention and treatment of secondary injury is the main goal of neuro-critical care. Identifying early signs of neurological deterioration is a challenge in the neuro-ICU. Early warnings could allow for preventive instead of reactive management, and may result in a more timely administration of therapy. In a retrospective study TBI patients with diffuse injury were found to likely benefit from different CPP therapy than those with mass lesions [48]. Predictive models could be important tools for clinicians to guide decision making. Early signs of imminent intracranial hypertension in severe TBI can be detected through advanced time series analysis of ICP and ABP combined in a machine learning model. It is striking that loss of cerebrovascular autoregulation was one of the main predictors in these models [49], a finding that has been confirmed in other studies [50,51]. In SAH, heart rate variability analysis was used to predict delayed cerebral ischemia and infections [52]. These predictive models are not yet available at the bedside, and their further development, implementation and validation could be done in a Big Data research platform.

Prediction of clinical outcome.

In the neuro-ICU, prognostic information can be used to guide family counseling, assess treatment effectiveness and allow efficient design of RCTs. The Glasgow Coma Score [53] and the Marshall CT score have been used to identify patients at risk for worse outcome, or as stratification for clinical trials [54]. The IMPACT [55] and CRASH (Corticosteroid Randomization After Significant Head Injury) [56] models have been rigorously designed and validated externally [57–60]. Time-series analysis of physiological monitoring during the first 24 hours in the ICU could improve the performance of these models [49]. Developing such models involves more than the naïve application of a black box algorithms, and should be constructed using proper statistical methods for selection of relevant features [61] with input from domain experts [62], and likewise following proper internal and external validation [63]. In order to determine the clinical value of a predictive model, not only the discrimination, but also the calibration, followed by a decision curves analysis, should be done [64] .

BIG DATA ANALYSIS AND CLINICAL RESEARCH

Most RCTs on neuro-protective strategies in the neuro-critical care unit have been negative [65]. The exact reasons for this are diverse, including insufficient preclinical experimental work, incomplete (patho)physiological understanding or methodological flaws. Likewise, the primary endpoints might not have been sensitive enough, or might have missed a link with pathophysiology. In general, it proves to be very challenging to design RCTs that take into account population heterogeneity, and to delineate those subgroups that might benefit most from a certain intervention. On the one hand, randomizing patients is still the best way to establish a causal inference between an intervention and outcome. On the other hand, ethical, financial or compliance constraints can limit the feasibility of translating a research question into a RCT. Big data has been proposed as a complement to RCTs [66,67]. Adaptive clinical trials could be a way forward, where a trial is designed in such a way that it can 'learn' to identify subgroups or conditions in which the intervention could be beneficial. For those research questions where an RCT is not feasible, Big Data research could be an alternative.

CONCLUSIONS

Big Data can give a new perspective on the many challenges that we face in medicine and neuro-critical care. Researchers and clinicians need to be aware of the opportunities, but at the same time will need to look beyond the hype. Proper data organization and structuring, together with the design of appropriate analytic tools, will be of key importance [68]. In addition to these data analysis modalities, new ways of presenting individualized predictions and treatment recommendations to healthcare providers will have to be designed and validated [69]. Hence, the processing and analysis of the large amount of patient-related information stored in well-designed databases has the potential to improve neuro-critical care.

KEYPOINTS

- Big Data research should begin with a clear understanding of the value it will bring.
- Existing databases in neuro-critical care are not well suited for Big Data applications. A particular focus should be made to develop large, multicenter, high resolution and quality databases.
- Big Data hold a great promise to personalize patient care through clinical decision support tools based on robustly designed machine learning models.
- Big Data research is not an easy alternative to difficult clinical trials.
- RCTs and Big Data are complementary; the latter can identify patient groups that may benefit more from RCTs, or can be used to address specific research questions when RCTs are not feasible.

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REFERENCES

1. Marr B. Why only one of the 5 Vs of big data really matters (Blog). [Internet]. 2015 [cited 2015 Nov 6]. Available from: http://www.ibmbigdatahub.com/blog/why-only-one-5-vs-big-data-really-matters

2. Laney D. META Delta. Appl Deliv Strateg. 2001;949(February 2001):4.

3. Slack E. Lowering the Cost of Deleting Data [Internet]. 2014 [cited 2015 Nov 22]. Available from: http://storageswiss.com/2014/02/10/lowering-the-cost-of-deleting-data/

4. Morris G, Gardner R. Computer applications. In: Hall J, Schmidt G, Wood L, editors. Principles of critical care. McGraw-Hill: New York; 1992. p. 500–14.

5. Le Roux P, Menon DK, Citerio G, et al. Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care. Intensive Care Med. 2014;40(9):1189–209.

6. Vespa P, Menon D, Le Roux P. The International Multi-disciplinary Consensus Conference on Multimodality Monitoring: Future Directions and Emerging Technologies. Neurocrit Care. 2014;21(S2):270–81.

7. Citerio G, Park S, Schmidt JM, et al. Data Collection and Interpretation. Neurocrit Care. 2015;22(3):1–9.

8. Bourne PE, Lorsch JR, Green ED. Sustaining the big-data ecosystem. Nature. 2015;527(7576):S16–17.

9. Shukla SK, Murali NS, Brilliant MH. Personalized medicine going precise: from genomics to microbiomics. Trends Mol Med. 2015;21(8):461–2.

10. Grumbach K, Lucey CR, Johnston CS. Transforming from centers of learning to learning health systems: the challenge for academic health centers. Jama 2014;311(11):1109–10.

11. Halamka J. Early experiences with big data at an academic medical center. Heal Aff (Millwood). 2014;33(7):1132–8.

12. MIT editors. Business Report: Data-driven Health Care. MIT Technol Rev. 2014;117:1–19.

13. Thompson G, O'Horo JC, Pickering BW, et al. Impact of the Electronic Medical Record on Mortality, Length of Stay, and Cost in the Hospital and ICU: A Systematic Review and Metaanalysis. Crit Care Med 2015;43(6):1.

14. Schmidt JM, De Georgia M. Multimodality Monitoring: Informatics, Integration Data Display and Analysis. Neurocrit Care. 2014;21(S2):229–38.

15. Sivaganesan A, Manley GT, Huang MC. Informatics for Neurocritical Care: Challenges and Opportunities. Neurocrit Care. 2014;20(1):132–41.

16. De Georgia MA, Kaffashi F, Jacono FJ, et al. Information technology in critical care: review of monitoring and data acquisition systems for patient care and research. ScientificWorldJournal. 2015;2015:727694.

17. Hravnak M, Chen L, Dubrawski A, et al. Real alerts and artifact classification in archived multi-signal vital sign monitoring data: implications for mining big data. J Clin Monit Comput. Springer Netherlands; 2015;

18. Pugin J. Profiling genes in the ICU: Are we there yet? Intensive Care Med. 2008;34(8):1357–9.

19. Herr T, Freimuth R, Hartzler A, et al. A conceptual model for translating omic data into clinical action. J Pathol Inform. 2015;6(1):46.

20. Maas AIR, Harrison-Felix CL, Menon D, et al. Standardizing data collection in traumatic brain injury. J Neurotrauma. 2011;28(2):177–87.

21. Marmarou A, Lu J, Butcher I, et al. IMPACT Database of Traumatic Brain Injury: Design And Description. J Neurotrauma. 2007;24(2):239–50.

22. Piper I, Citerio G, Chambers I, et al. The BrainIT group: concept and core dataset definition. Acta Neurochir (Wien). 2003;145(8):615–29.

23. Saeed M, Lieu C, Raber G, et al. MIMIC II: a massive temporal ICU patient database to support research in intelligent patient monitoring. Comput Cardiol. 2002;29:641–4.

24. International Initiative for Traumatic Brain Injury Research. [Internet]. 2014. Available from: http://intbir.nih.gov/

25. Maas AIR, Menon DK, Steyerberg EW, et al. Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI). Neurosurgery. 2015;76(1):67–80.

26. Güiza F, Van Eyck J, Meyfroidt G. Predictive data mining on monitoring data from the intensive care unit. J Clin Monit Comput 2013;27(4):449–53.

27. Holzinger A, Dehmer M, Jurisica I. Knowledge Discovery and interactive Data Mining in Bioinformatics - State-of-the-Art, future challenges and research directions. BMC Bioinformatics. BioMed Central Ltd; 2014;15(Suppl 6):I1.

28. Esfandiari N, Babavalian MR, Moghadam A-ME, et al. Knowledge discovery in medicine: Current issue and future trend. Expert Syst Appl. Elsevier Ltd; 2014;41(9):4434–63.

29. Brain Trauma Foundation. Guidelines for the Management of Severe Traumatic Brain Injury 3rd Edition. J Neurotrauma. 2007;24(212):1–106.

30. Cooper D, Rosenfeld J. Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med. 2011;364:1493–502.

31. Chesnut RM, Temkin N, Carney N, et al. A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury. N Engl J Med 2012;367(26):2471–81.

32. Vik A, Nag T, Fredriksli OA, et al. Relationship of “dose” of intracranial hypertension to outcome in severe traumatic brain injury. J Neurosurg. 2008 Oct;109(4):678–84.

*33. Lazaridis C, DeSantis SM, Smielewski P, et al. Patient-specific thresholds of intracranial pressure in severe traumatic brain injury. J Neurosurg 2014;120(4):893–900.

This study is the first to suggest that autoregulation may impact the ability to tolerate increased ICP.

**34. Güiza F, Depreitere B, Piper I, et al. Visualizing the pressure and time burden of intracranial hypertension in adult and paediatric traumatic brain injury. Intensive Care Med 2015 Apr;41:1067–76.

The authors introduce an interesting visualization tool that shows the relation between varying levels of ICP, duration, and outcome.

35. Bouma G, Muizelaar J. Cerebral blood flow, cerebral blood volume, and cerebrovascular reactivity after severe head injury. J Neurotrauma. 1992;9(Suppl 1):S333–48.

36. Budohoski KP, Czosnyka M, Kirkpatrick P, et al. Clinical relevance of cerebral autoregulation following subarachnoid haemorrhage. Nat Rev Neurol. 2013;9(3):152–63.

37. Petersen NH, Ortega-Gutierrez S, Reccius A, et al. Dynamic cerebral autoregulation is transiently impaired for one week after large-vessel acute ischemic stroke. Cerebrovasc Dis 2015;39(2):144–50.

38. Pham P, Bindra J, Chuan A, et al. Are changes in cerebrovascular autoregulation following cardiac arrest associated with neurological outcome? Results of a pilot study. Resuscitation. 2015;96:192–8.

39. Taccone FS, Castaneres-Zapatero D, Peres-Bota D, et al. Cerebral autoregulation is influenced by carbon dioxide levels in patients with septic shock. Neurocrit Care. 2010;12(1):35–42.

40. Kirsch JD, Mathur M, Johnson MH, et al. Advances in transcranial Doppler US: imaging ahead. Radiographics 2013;33(1):E1–14.

*41. Czosnyka M, Miller C. Monitoring of Cerebral Autoregulation. Neurocrit Care. 2014;21(S2):95–102.

A very clear review that explains the principles and perspectives of autoregulation monitoring, indications, and how this can be used to guide therapy.

42. Czosnyka M, Smielewski P, Kirkpatrick P, et al. Continuous assessment of the cerebral vasomotor reactivity in head injury. Neurosurgery. 1997;41(1):11–9.

43. Steiner L a., Czosnyka M, Piechnik SK, et al. Continuous monitoring of cerebrovascular pressure reactivity allows determination of optimal cerebral perfusion pressure in patients with traumatic brain injury. Crit Care Med. 2002 Apr;30(4):733–8.

44. Aries MJH, Czosnyka M, Budohoski KP, et al. Continuous determination of optimal cerebral perfusion pressure in traumatic brain injury*. Crit Care Med. 2012;40(8):2456–63.

45. Depreitere B, Güiza F, Van den Berghe G, et al. Pressure autoregulation monitoring and cerebral perfusion pressure target recommendation in patients with severe traumatic brain injury based on minute-by-minute monitoring data. J Neurosurg. 2014;120(June):1451–7.

*46. Weersink CSA, Aries MJH, Dias C, et al. Clinical and Physiological Events That Contribute to the Success Rate of Finding “Optimal” Cerebral Perfusion Pressure in Severe Brain Trauma Patients. Crit Care Med. 2015;43(9):1952–63.

The first study that has investigated the clinical reasons behind failure to determine CPPopt

47. Dias C, Silva MJ, Pereira E, et al. Optimal Cerebral Perfusion Pressure Management at Bedside: A Single-Center Pilot Study. Neurocrit Care. 2015;92–102.

48. Johnson U, Lewén A, Ronne-Engström E, et al. Should the Neurointensive Care Management of Traumatic Brain Injury Patients be Individualized According to Autoregulation Status and Injury Subtype? Neurocrit Care. 2014;21(2):259–65.

49. Güiza F, Depreitere B, Piper I, et al. Novel methods to predict increased intracranial pressure during intensive care and long-term neurologic outcome after traumatic brain injury: development and validation in a multicenter dataset. Crit Care Med 2013;41(2):554–64.

50. Kim N, Krasner A, Kosinski C, et al. Trending autoregulatory indices during treatment for traumatic

brain injury. J Clin Monit Comput. Springer Netherlands; 2015;

51. Pineda BA, Qadri MJ, Kosinski C, et al. Developing a Continuous Hemodynamic Autoregulation Monitor. In: Biomedical Engineering Conference (NEBEC), 2015 41st Annual Northeast IEEE. 2015. p. 1–2.

52. Schmidt JM, Sow D, Crimmins M, et al. Heart Rate Variability for Preclinical Detection of Secondary Complications After Subarachnoid Hemorrhage. Neurocrit Care. 2014;20(3):382–9.

53. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet. 1975;1(7905):480–4.

54. Lawrence F. Marshall, Sharon Bowers Marshall, Melville R. Klauber, et al. A new classification of head injury based on computerized tomography. J Neurosurg. 1991;75(1s):S14–20.

55. Maas AIR, Marmarou A, Murray GD, et al. Prognosis and clinical trial design in traumatic brain injury: the IMPACT study. J Neurotrauma. 2007;24(2):232–8.

56. MRC CRASH Trial Collaborators. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. Bmj. 2008;336(7641):425–9.

57. Majdan M, Lingsma HF, Nieboer D, et al. Performance of IMPACT, CRASH and Nijmegen models in predicting six month outcome of patients with severe or moderate TBI: an external validation study. Scand J Trauma Resusc Emerg Med. 2014;22(1):68.

58. Han J, King NKK, Neilson SJ, et al. External Validation of the CRASH and IMPACT Prognostic Models in Severe Traumatic Brain Injury. J Neurotrauma. 2014;7:1–7.

59. Harrison D a., Griggs K a., Prabhu G, et al. External Validation and Recalibration of Risk Prediction Models for Acute Traumatic Brain Injury among Critically Ill Adult Patients in the United Kingdom. J Neurotrauma. 2015;32(19):1522–37.

60. Lingsma HF, Yue JK, Maas AIR, et al. Outcome Prediction after Mild and Complicated Mild

Traumatic Brain Injury: External Validation of Existing Models and Identification of New Predictors Using the TRACK-TBI Pilot Study. J Neurotrauma. 2015;32(2):83–94.

*61. Stein SC, Attiah MA. Clinical Prediction and Decision Rules in Neurosurgery. Neurosurgery. 2015;77(2):149–56.

This pubication describes thoroughly how prediction models should be derived, validated, evaluated, and used in practice.

62. McAfee A, Brynjolfsson E. Big Data. The management revolution. Harvard Buiness Rev. 2012;90(10):61–8.

**63. Steyerberg EW, Harrell Jr. FE. Prediction models need appropriate internal , internal-external , and external validation. J Clin Epidemiol. 2015;(October):5–8.

Internal-external validation is a novel and promising technique to validate prediction models in a more robust way

**64. Fitzgerald M, BR S, RJ L. Decision curve analysis. Jama. 2015;313(4):409–10.

Athough they have been introduced in 2006, decision curves are still infrequently used to assess the clinical benefit of a prediction model. This very well-written review provides a clear explanation how they can be used in clinical medicine.

65. Stocchetti N, Taccone FS, Citerio G, et al. Neuroprotection in acute brain injury: an up-to-date review. Crit Care [Internet]. 2015;19(1):186.

**66. Angus DC. Fusing Randomized Trials With Big Data The Key to Self-learning Health Care Systems ? Jama. 2015;314(8):767–8.

Great viewpoint and perspective how Big Data and RCTs can be complementary .

*67. Lazaridis C, Maas AIR, Souter MJ, et al. Alternative Clinical Trial Design in Neurocritical Care. Neurocrit Care. 2015;22(3):378–84.

The evidence behind treatment recommendation guidelines is disapointingly poor. Comparitive effectiveness research is a potential method to deliver new insights in neurocritical care.

68. Ghassemi M, Celi L, Stone DJ. State of the art review: the data revolution in critical care. Crit Care 2015;19(1):118.

69. Celi LA, Csete M, Stone D. Optimal Data Systems: The future of clinical predictions and decision support. Curr Opin Crit Care. 2014;20(5):573–80.

Figure 1

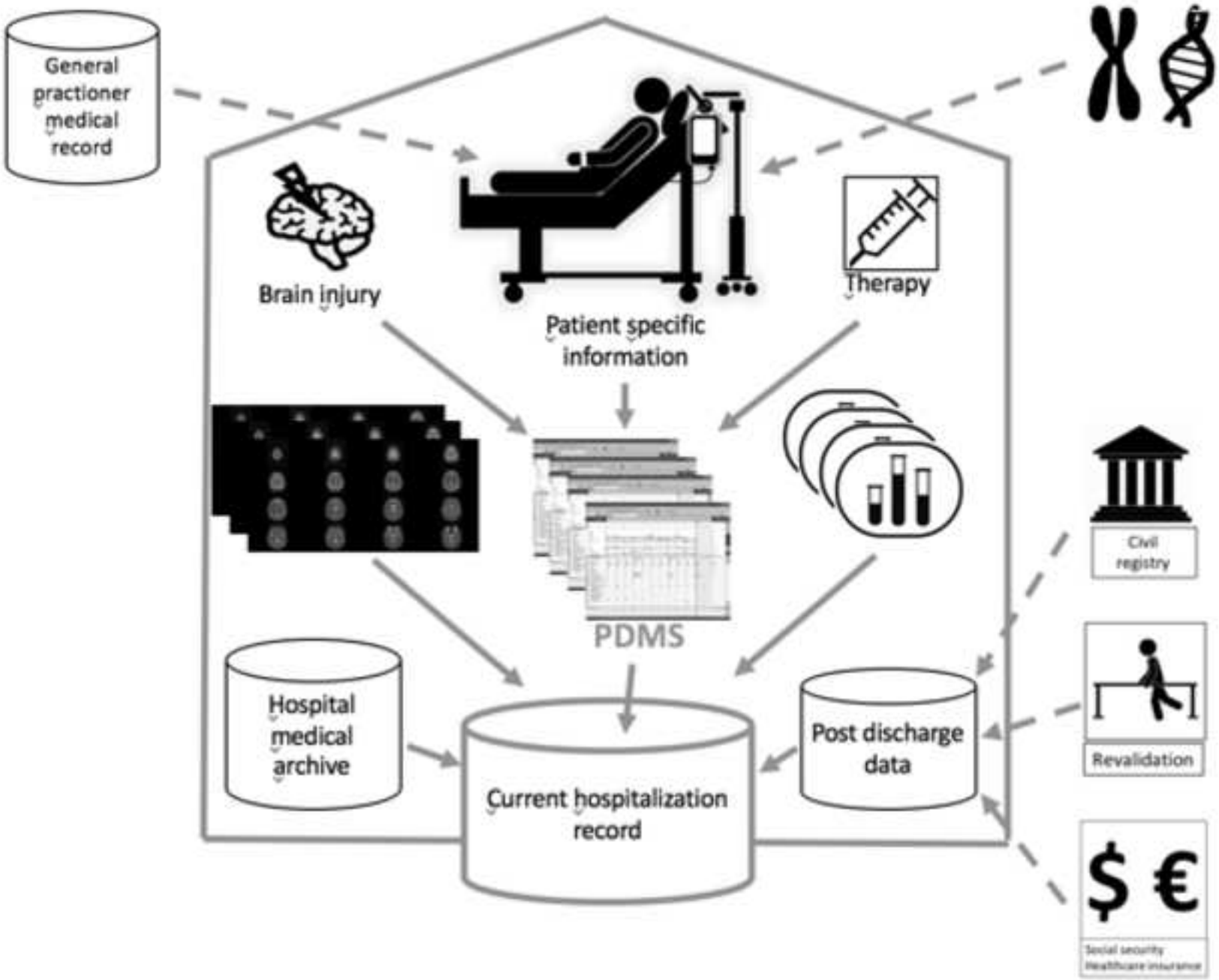
General practioner medical record
Brain injury
Patient specific information
Therapy
PDMS
Hospital medical archive
Current hospitalization record
Post discharge data
Civil registry
Revalidation
$ €

Figure 1: Schematic representaion of the relevant healthcare information that could be collected during and after the admission of a patient to the neuro-ICU. Patient specific information, can refer to demographic data, age and gender, medical history, co-morbitities, but also to the data collected during his ICU stay such as monitoring data. These data are typically collected in the electronic health record of the ICU, called the patient data management system or PDMS. Data from the PDMS, together with the radiological examinations and lab data, are stored in the hospitalization record of the patient. Ideally, post discharge data from outpatient visits, reports from revalidation, social security or healthcare insurance information regarding degree of invalidity and dependence, as well as the civil registry where mortality data can be retrieved, should also be added tot he post-discharge data of the patient.

Table 1 including legend

Table1: The five V's of big data	
Volume	The large amount of data generated
Velocity	The speed at which data are generated, transmitted, and processed
Variety	The different types and formats of data • Structured and unstructured data • Text • Numeric data • Images, video, audio • …
Veracity	The reliability, quality, accuracy, or trustworthiness of the data
Value	The use of these data for a specific benefit , or the potential ability to turn data into value

Table 1: Big data is often defined as the three, four, or five V's. The importance of the fifth V, Value, is being increasingly recognized.